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Heritable and Life-style Determinants of Bone Mineral Density

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ABSTRACT

Familial resemblance in bone mineral density at five skeletal sites was measured among 160 adult members of 40 families. Each family included a postmenopausal mother, one premenopausal daughter, one son, and the children's father. Similarities in selected life-style factors thought to influence bone density, such as physical activity, smoking, alcohol use, and diet, were also evaluated. Bone density was measured by dual-energy (total body, femoral neck, and lumbar spine) or single-photon (radius and os calcis) absorptiometry. Correlation coefficients between the midparent Z score and offspring Z scores of bone mineral density ranged from 0.22 to 0.52 among daughters and from 0.27 to 0.58 among sons. Adjustment of bone density for age, height, weight, and significant life-style or environmental factors yielded heritability estimates for the five skeletal sites between 0.46 and 0.62. That is, 46–62% of variance in bone density was attributable to heredity. Most estimates derived from the group of daughters were similar to those from the sons. These observations provide support for a significant contribution of heredity to bone density. However, an individual's life-style may account for a potentially large proportion of the nonheritable variance in bone density.

INTRODUCTION

The majority of studies of bone density among parents and their children,[1-7] twins,[8-12] and healthy relatives of individuals with osteoporosis[13,14] demonstrate familial resemblances in bone density that strongly suggest a genetic contribution.

As is generally recognized, familial resemblance is not necessarily due entirely to genetic transmission of a trait.[15] Families may have a common environment, for example, life-style habits, that contributes to the hereditary appearance of bone density if these habits also influence bone density. Calcium intake, physical activity, smoking, and alcohol are a few of the numerous life-style factors putatively associated with variability in bone density and rates of bone loss. The importance of dietary calcium in achieving and maintaining adequate bone density is not universally agreed upon. Relationships between calcium intake and bone density or bone loss have been shown in some but not all segments of the population. Bone loss among women who are premenopausal[16] or beyond the first 5 years of menopause[17] is reduced at some skeletal sites by increased calcium intake. Demonstrable effects of calcium on bone loss may occur primarily in individuals whose usual intake is well below recommended levels.[17]

Greater physical activity has also been associated with increased bone density. There is controversy, however, over the intensity and type of exercise needed for this benefit. Strenuous activity, whether or not it is weight bearing, appears beneficial to bone density,[18-20] but few cross-sectional studies have suggested a similar effect at low and moderate activity levels,[21] which typify the majority of adults in the population. Smoking is associated with reduced bone density[22-24] and accelerated loss.[25] The effect of moderate alcohol consumption is uncertain.[26-28]

Similarities in diet, physical activity, smoking, and drinking between spouses or between parents and offspring have been reported. Intakes of many nutrients are correlated between husbands and wives,[29] although the

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extent of correspondence for calcium is unknown. One study has reported no relationship between calcium intakes of mothers and daughters.[3] Coffee consumption of college-aged adults was correlated with that of both parents.[30] A father's physical activity level appeared to influence those of both sons and daughters.[31] Smoking behavior of college students two to three decades ago was related to the smoking status of the parent of the same sex,[32] but no significant concordance was found in a more recent study.[31] At moderate consumption levels, alcohol intake of women was related to use by both parents and intake among sons was predicted by the mother's drinking habit.[31] The cumulative effect of these shared life-style habits on estimates of familial resemblance of bone density may be important.

Although there is little doubt that genetics plays a role in determining the variability in bone density, the relative importance of genetic and environmental factors remains unclear. In intergenerational studies, estimates of the heritability of bone density (the proportion of total variance attributable to genetic effects) have been similar, approximately 50–70%.[1–3] Other estimates, all from twin studies, have ranged as high as 80–90%.[6–10] It is important to know which range of estimates reflects the heredity of bone density, that is, whether determinants are predominantly genetic or whether a substantial proportion is related to environment, including life-style. Life-style factors are open to intervention.

The objectives of this study were to measure familial resemblance of bone density of female and male members of 40 families, identify environmental factors the families share, and evaluate the impact of these factors on the degree of resemblance among the members. Heritability indices were used to measure familial resemblance in bone density at five skeletal sites.

MATERIALS AND METHODS

Subjects

The 160 volunteers in the study were members of 40 families, each of which included a postmenopausal mother, one adult premenopausal daughter, one adult son, and the children's biologic father. Entry criteria included good health, European ancestry, and no use within the past year of any of the following: corticosteroids, anticoagulant or antiseizure medications, and postmenopausal estrogen (however, 10 of the mothers had used estrogen prior to 1 year before participation). Individuals were free of conditions that affect bone metabolism or absorption of any nutrient. Current use of oral contraceptives was not an exclusion criterion. A total of 17 mothers were also participants in a series of nutritional intervention trials.[17,33] None of the daughters was pregnant at the time of the study. All volunteers gave informed consent. The protocol was approved by the Human Investigations Review Committee of Tufts University. The study population is described in Table 1.

Measurements

Height and weight were measured without shoes, height with a wall-mounted ruler and weight on a digital scale with the volunteer wearing either a hospital gown or light street clothes. Truncal thickness was measured at the level of the umbilicus while the volunteer was prone.

Bone mineral density (BMD) of lumbar vertebrae L2–4, femoral neck, and total body were measured by dual-energy absorptiometry (Lunar Model DPX, Lunar Corp.) and analyzed with Lunar software Version 3.1. The coefficients of variation (CVs) of the spine, femoral neck, and total-body BMD were 1, 2.1, and 0.6%, respectively.[34] Os calcis density was measured with a single-photon absorptiometer (Osteon Corp). BMD of the radius (two-thirds distal site) was measured with a single-photon absorptiometer (Lunar Model SP2). Coefficients of variation at the heel and radius were 1.5 and 1%, respectively (unpublished observations).

For the 17 mothers in the intervention trials, the BMD values used in all analyses were those measured at trial baseline to avoid any effect of intervention on the correlations within these families. Spine and hip measurements of these women were made with a dual-photon absorptiometer (Lunar DP3). The CV of the spine on this machine was 2% and that of the femoral neck, 3%.[35] These measurements had been corrected for ^{153}Gd source strength, and spine BMD was also corrected for truncal thickness as described previously.[36] The mean lengths of time between baseline scans and the present study ranged from 6 months (total body) to 2.8 years (spine and hip).

An aluminum phantom was scanned on the DPX in a mixture of oil and water at a ratio of 30% oil and 70% water at six equidistant thicknesses between 15.2 and 27.9 cm, a range that simulated truncal thickness observed in this laboratory. Phantom readings at the lowest thickness were significantly lower than readings from 17.8 through 7.9 cm.[35] Corrections were made to 23 individuals with truncal thickness below 17.8 cm by assuming BMD increased linearly by 0.5% per cm up to 17.8 cm and was constant at all higher thicknesses. The correction resulted in an average increase to spine density of 0.4% in those individuals. The magnitude of the correction was greater among those with low weight (1% change in BMD) and lowest among heavier participants (less than 0.1% change) in this range of thicknesses.

The number of family sets with complete scans differed by skeletal site. There were 33 families with complete bone data at the radius, 32 at the os calcis, and 37 families with complete bone data at the spine, femur, and total body. The most frequent reasons for missing or bad scan data were subjects who were too large for the scan equipment and equipment malfunction.

Current cigarette and alcohol consumption, reproductive history and oral contraceptive use, and present use of medications, vitamins, and mineral supplements were assessed by questionnaire. Alcohol consumption was defined as drinks per week, with 1 drink equivalent to 1 ounce of liquor, 4 ounces of wine, or 12 ounces of beer. Menopausal age was adjusted for the 10 mothers who used post-

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TABLE 1. DESCRIPTION OF STUDY POPULATION[a]

	Mother	*Father*	*Daughter*	*Son*
n	40	40	40	40
Age, years	60 ± 6	63 ± 6	31 ± 6	32 ± 5
	59	64	32	32
Weight, kg	69 ± 13	83 ± 13	66 ± 15	84 ± 14
	66	80	60	84
Height, cm	161 ± 7	175 ± 8	163 ± 7	179 ± 8
	162	174	162	178
Body mass index, kg/cm²	26.6 ± 4.6	27.1 ± 3.8	24.6 ± 5.6	26.3 ± 3.8
	25.2	26.4	22.6	25.7
Calcium intake, mg/day	740 ± 416	852 ± 523	801 ± 493	951 ± 536
	601	746	735	871
Caffeine intake, mg/day	335 ± 381	612 ± 865	309 ± 329	401 ± 426
	222	357	210	231
Physical activity, minutes/day	38 ± 31	44 ± 42	46 ± 50	66 ± 71
	31	35	29	43
Current alcohol use, drinks	4 ± 8	6 ± 10	3 ± 5	4 ± 5
per week[b]	1	2	1	3
Current cigarette use				
%	8	8	13	23
Packs/day[c]	0.8 ± 0.3	0.9 ± 0.2	0.8 ± 0.2	1.2 ± 0.9
Bone mineral density, g/cm²[d]				
Total body	1.14 ± 0.09	1.23 ± 0.08	1.17 ± 0.07	1.31 ± 0.08
Radius	0.67 ± 0.08	0.79 ± 0.08	0.69 ± 0.06	0.82 ± 0.08
Os calcis	0.50 ± 0.09	0.62 ± 0.09	0.56 ± 0.08	0.65 ± 0.10
Femoral neck	0.89 ± 0.11	0.92 ± 0.13	0.97 ± 0.08	1.06 ± 0.15
Spine	1.16 ± 0.15	1.19 ± 0.21	1.21 ± 0.14	1.23 ± 0.14

[a]Mean ± SD and median.
[b]One drink is equivalent to 1 ounce of liquor, 4 ounces of wine, or 12 ounces of beer.
[c]Current smokers only.
[d]Bone density adjusted for weight and height.

menopausal estrogen prior to 1 year before participation by subtracting the years of estrogen use from the self-reported age at menopause.

Dietary intakes of calcium and caffeine within the previous 6 months were assessed by a food frequency questionnaire.[17] Total intake of calcium was obtained by adding dietary and supplemental sources. Dietary intakes of the 17 mothers in the previous trials that were obtained before their enrollment were used in statistical analyses.

Physical activity level was estimated by a questionnaire.[37] The average amount of time spent in 20 sports and leisure activities was obtained for the appropriate current age period (ages 14–21, 22–34, 35–50, or 50 and above) and converted to kilocalories per kilogram body weight by multiplying time and an intensity value[38] for each activity item.

Statistical methods

Age and/or body size effects on bone mineral density were removed by adjusting each individual's BMD to the means of these three variables in the appropriate sex and generation group. Generational and sex differencs in BMD corrected for body size were evaluated with two-way analysis of variance.

BMD *Z* scores after adjustment for age, weight, and height were computed separately for the mothers, fathers, daughters, and sons based on the means and standard deviations in each group. For the mothers on whom spine and hip densities were measured on a different absorptiometer, *Z* scores at these sites were based on measurements specific to that machine.

Distributions of caffeine intake, physical activity, and alcohol use were transformed with the square-root function. The results of the transformations were reduced skewness and less heterogeneity in the variances among the family member groups. Cigarettes per day was coded into categories of none, less than 1 pack, 1–2 packs, or 2+ packs per day.

Pearson correlation coefficients of Spearman rank correlations of BMD *Z* scores and life-style factors were computed between all possible family member pairs. In correlation matrices for each variable, there were six possible comparisons among the four family member groups. The observed *p* values were adjusted by multiplying each by 6 to compensate for the multiple comparisons.

Forward regression analyses identified the significant environmental factors that explained variance in bone density within each type of family member. Age, weight, and height were forced into the models, and the following envi-

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ronmental variables were allowed to enter if the p value was 0.15 or less. In all four family member groups, calcium intake, caffeine intake, physical activity, packs per day, and drinks of alcohol per week were considered for inclusion. For the mothers and daughters, additional variables considered were parity (number of live births), average length of breast-feeding, and oral contraceptive use and, for mothers only, years since menopause.

A second set of adjusted BMD values, adjusted for age, body size, and any environmental factors that were significant at $p < 0.05$ in the forward regression analyses, was derived and converted to Z scores.

The total variance of a phenotypic trait in a population can be divided into genetic and nongenetic variances. Genetic variance is further broken down into additive (that which is transmissible between generations) and nonadditive (which includes dominance variance and variance due to interactions among multiple loci) components. The relationships among family members determine whether the covariance of the trait between relatives represents only the additive component or the sum of additive and nonadditive genetic variances. For example, the comparison of parents with offspring yields additive genetic variance because parents do not pass on dominance deviations to their children. In contrast, the covariance between full siblings is a function of additive and nonadditive variances and, furthermore, the common environment. Common environment is difficult to separate from the genetic components, and its presence leads to an imprecise estimate of genetic variances. It is generally assumed that variability due to common environment exerts a greater effect on the resemblance of siblings than on other types of relationships, especially those involving different generations.[15]

The heritability index describes the ratio of genetic to total variance. Heritability indices that include only additive genetic variance (e.g., parent-offspring comparisons) in the numerator are termed "heritability in the narrow sense" (h_N^2). A heritability index that is estimated from full siblings, and thus includes nonadditive genetic variance, yields heritability in the broad sense (h^2). If dominance variance and/or common environment contribute substantially to the resemblance of siblings, the h^2 estimates are higher than h_N^2.

Heritability in the narrow sense was estimated in this study by the regression coefficient (b_P) of the parent's BMD Z scores in models in which the BMD Z score of offspring was the dependent variable; that is, $BMD_O = b_i + b_P(BMD_P)$. This regression coefficient, by definition, is the ratio of covariance between parent and offspring to variance of the parent, which represents total variance in the phenotype. BMD_O can be that of one child or the mean of all children in a family. BMD_P represents the midparental BMD Z score.

Heritability in the broad sense (h^2) was estimated as twice the intraclass correlation coefficient of the sons and daughters from analyses of variance of BMD Z scores.

Correlations and heritability of BMD Z scores were calculated for family sets in which no member was missing that type of scan.

RESULTS

The mothers ranged in age from 43 to 71 years, averaged 10 ± 7 (standard deviation, SD) years since menopause, had 4 ± 1 children, and breast-fed each child 2 ± 3 months. The age range of the fathers was 44–75, of the daughters, 21–45, and of the sons, 21–44 years. The mean number of live births to the daughters was 1 ± 1. Significant generation and sex differences ($P < 0.05$) in BMD adjusted for weight and height were seen at each of the total-body, radius, heel, and hip sites. In contrast, the age effect at the spine was marginally significant ($p = 0.09$), and no sex difference was observed in either age group.

Midparent BMD Z scores (adjusted for age, weight, and height) were positively correlated with those of daughters and sons (Table 2). Correlations between individual parent and offsrping combinations are also shown. The midparent values in general equaled or exceeded the correlations between offspring and each parent.

Height of the sons was significantly correlated with heights of both parents, and the daughters' weight and body mass index resembled those of their mothers (Table 3). Alcohol was the only environmental factor for which levels in mothers and fathers were significantly correlated ($r = 0.57$, $p < 0.01$).

Results of the regressions of body size and environmental factors are shown in Table 4. Controlling for age and body size, the significant predictors of bone density at each site varied among the different family members. However, physical activity was associated with BMD among fathers, mothers, and daughters at one or more sites, and reproductive factors were related to BMD in the mothers and daughters at several sites.

Estimates of heritability of bone density adjusted for age, weight, and height obtained from sibling pairs were compared to those obtained from the parent-offspring comparison (Table 5). The broad estimates of heritability (siblings) were higher than h_N^2 (parent-offspring) at the total body, radius, and heel by 16, 34, and 12%, respectively. At the femoral neck and spine, however, the h_N^2 was larger in magnitude.

Adjustment of h_N^2 from the midparent-midoffspring analyses for environmental factors reduced the indices by 3–9% (Table 6). When h_N^2 was estimated separately from daughters or sons, the indices were comparable between the sexes, with the exception of the hip, both before and after adjustment.

DISCUSSION

Familial associations in bone density were observed between parents and their daughters and sons at most skeletal sites measured. To our knowledge, this study is the first to report familial correlations and heritability estimates for the total-body and os calcis sites. This study also extends observations at multiple skeletal sites to mother-son and father-son pairs.

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TABLE 2. CORRELATIONS OF BONE DENSITY Z SCORES AMONG FAMILY MEMBERS[a]

	Daughter	*Son*
Total body		
Mother	0.54[b]	0.57[b]
Father	0.11	0.24
Daughter	—	0.40
Midparent	0.46[c]	0.54[d]
Radius		
Mother	0.35	0.27
Father	0.40	0.23
Daughter	—	0.30
Midparent	0.47[c]	0.27
Os calcis		
Mother	0.50[c]	0.51[d]
Father	0.24	0.23
Daughter	—	0.45[c]
Midparent	0.52[c]	0.51[c]
Femoral neck		
Mother	0.40	0.47[c]
Father	−0.12	0.31
Daughter	—	0.29
Midparent	0.22	0.58[b]
Lumbar spine		
Mother	0.30	0.28
Father	0.16	0.24
Daughter	—	0.10
Midparent	0.34	0.37

[a]BMD is adjusted for age, weight and height. Indicated values show r significantly greater than 0.
[b]$p < 0.001$.
[c]$p < 0.05$.
[d]$p < 0.01$.

TABLE 3. CORRELATIONS OF BODY SIZE AND LIFE-STYLE FACTORS AMONG FAMILY MEMBERS[a]

	Daughter	*Son*
Height		
Mother	0.38	0.60[b]
Father	0.26	0.58[b]
Daughter	—	0.32
Midparent	0.39	0.72[b]
Weight		
Mother	0.49[c]	0.28
Father	0.38	0.38
Daughter	—	0.15
Midparent	0.57[b]	0.44[c]
Body mass index		
Mother	0.59[b]	0.31
Father	0.23	0.25
Daughter	—	0.18
Midparent	0.57[b]	0.37
Calcium intake		
Mother	0.29	0.25
Father	0.09	−0.05
Daughter	—	0.16
Midparent	0.24	0.11
Caffeine intake		
Mother	0.26	0.31
Father	0.24	0.14
Daughter	—	0.40[c]
Midparent	0.32	0.26
Physical activity		
Mother	0.33	−0.12
Father	−0.12	0.34
Daughter	—	0.20
Midparent	0.10	0.21
Drinks per week		
Mother	0.40	0.36
Father	0.37	0.27
Daughter	—	0.41[c]
Midparent	0.41[c]	0.32
Cigarettes per day		
Mother	−0.11	0.31
Father	−0.12	0.31
Daughter	—	0.18
Midparent	−0.14	0.38

[a]Spearman rank correlation coefficient presented for drinks per week and cigarettes per day; Pearson correlation coefficient for all others. Indicated values show r significantly greater than 0.
[b]$p < 0.001$.
[c]$p < 0.05$.

The heritable proportion of variance in BMD may be overestimated in family studies as a result of common environmental effects. The nonheritable proportion ($1 - h^2$) includes environment that is specific to an individual and measurement error. Through the adjustment of BMD measurements for life-style and reproductive factors, the extent to which BMD of parents and their children covaried was reduced. Thus some variance originally attributed to genetics was instead due to nongenetic factors. The reductions were small, as might be expected given the limited number of life-style variables significantly related to BMD and the modest correlations of life-style factors among family members. Identification and removal of variance due to additional common environmental factors not ascertained in this study may have a similar impact on heritability estimates.

Comparison of the broad and narrow estimates of heritability in this group of families was inconclusive. The broad estimate appeared to be higher than the narrow at three sites, suggesting that the resemblance of bone density between siblings was influenced by nonadditive genetic variance and/or common environment. The reverse was seen at the remaining two sites, however. A larger number of families is necessary to resolve this question.

Heritability estimates are unique to each population sample studied. It has been proposed that with increasing age, an individual's environment becomes more influential on bone and the familial association becomes less evident.[8] This may be especially important in women in whom the rapid rates of bone loss after menopause are a significant source of variability in bone density. If bone densities of parents and children could be measured at or

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TABLE 4. RESULTS OF REGRESSION ANALYSES ON BONE MINERAL DENSITY[a]

Mothers	B	r^2	*Fathers*	B	r^2
Total body		11			41
Age, years	−0.0007		Age, years	0.0017	
Weight, kg	0.0022[b]		Weight, kg	0.0040[c]	
Height, cm	0.0011		Height, cm	0.0007	
Intercept	0.8482		Activity (kcal/kg/day)$^{1/2}$	0.0308[c]	
			Intercept	0.6126	
Radius		7			18
Age, years	−0.0022		Age, years	−0.0002	
Weight, kg	−0.0001		Weight, kg	0.0013	
Height, cm	−0.0017		Height, cm	0.0033	
Calcium intake, g/day	0.0378[d]		Intercept	0.1176	
Intercept	1.0519				
Os calcis		56			27
Age, years	0.0005		Age, years	0.0014	
Weight, kg	0.0032[e]		Weight, kg	0.0029[d]	
Height, cm	−0.0040[d]		Height, cm	−0.0005	
Number of children	−0.0283[c]		Activity, (kcal/kg/day)$^{1/2}$	0.0331[d]	
Lactation, total months	0.0172[e]		Intercept	0.3155	
Alcohol, (drinks per week)$^{1/2}$	0.0249[e]				
Intercept	0.9196				
Femoral neck		24			24
Age, years	0.0029		Age, years	0.0001	
Weight, kg	0.0016		Weight, kg	0.0039[d]	
Height, cm	−0.0001		Height, cm	−0.0012	
Number of children	−0.0271[d]		Activity, (kcal/kg/day)$^{1/2}$	0.0411[d]	
Activity, (kcal/kg/day)$^{1/2}$	0.0497[d]		Intercept	0.7293	
Intercept	0.6299				
Spine		18			18
Age, years	0.0052		Age, years	0.0064	
Weight, kg	0.0037[b]		Weight, kg	0.0050[b]	
Height, cm	0.0024		Height, cm	−0.0030	
Activity, (kcal/kg/day)$^{1/2}$	0.0598[d]		Activity, (kcal/kg/day)$^{1/2}$	0.0605[d]	
Intercept	0.1083		Intercept	0.7885	
Daughters	B	r^2	*Sons*	B	r^2
Total body		48			31
Age, years	0.0006		Age, years	0.0015	
Weight, kg	0.0024[c]		Weight, kg	0.0048[c]	
Height, cm	0.0036[d]		Height, cm	−0.0019	
Number of children	−0.0225[d]		Intercept	1.1580	
Cigarettes, packs/day	−0.0422[d]				
Intercept	0.4285				
Radius		29			27
Age, years	−0.0025		Age, years	0.0029	
Weight, kg	−0.0006		Weight, kg	0.0028[d]	
Height, cm	0.0037[d]		Height, cm	0.0020	
Caffeine intake, (mg/day)$^{1/2}$	0.0028[d]		Intercept	0.1468	
Intercept	0.1553				
Os calcis		41			21
Age, years	−0.0025		Age, years	0.0009	
Weight, kg	0.0036[e]		Weight, kg	0.0036[d]	
Height, cm	0.0027		Height, cm	−0.0007	
Intercept	−0.0431		Intercept	0.4430	

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TABLE 4. (CONTINUED)

Daughters	B	r^2	*Sons*	B	r^2
Femoral neck		54			12
Age, years	−0.0001		Age, years	−0.0011	
Weight, kg	0.0008		Weight, kg	0.0048[b]	
Height, cm	0.0085[c]		Height, cm	−0.0009	
Number of children	−0.0246[d]		Intercept	0.8433	
Activity, (kcal/kg/day)$^{1/2}$	0.0295[d]				
Intercept	−0.4863				
Spine		42			17
Age, years	0.0016		Age, years	0.0032	
Weight, kg	0.0008		Weight, kg	0.0049[d]	
Height, cm	0.0071[d]		Height, cm	−0.0008	
Number of children	−0.0420[d]		Intercept	0.8579	
Calcium intake, g/day	−0.0983[d]				
Cigarettes, packs/day	−0.0907[d]				
Intercept	0.0798				

[a] B is the regression coefficient $\hat{\beta}$.
[b] $p < 0.1$.
[c] $p < 0.01$.
[d] $p < 0.05$.
[e] $p < 0.001$.

TABLE 5. ESTIMATES OF HERITABILITY OF BONE DENSITY

	Siblings[a]	*Midparent midoffspring*[b]
Total body	0.80	0.69
Radius	0.57	0.51
Os calcis	0.86	0.64
Femoral neck	0.63	0.70
Spine	0.35	0.50

[a] Heritability in the broad sense. Twice the intraclass correlation coefficients of daughters' and sons' BMD Z score (adjusted for age, weight, and height). Each heritability estimate is significantly greater than 0, $p < 0.05$.

[b] Heritability in the narrow sense. Regression coefficient of midoffspring BMD Z scores (adjusted for age, weight, and height) on midparent BMD Z scores. Each heritability estimate is significantly greater than 0, $p < 0.05$.

near their respective peaks, the heritability estimates would likely be different, and perhaps stronger, than in a sample with parents of more advanced ages, such as this.

Nevertheless, the correlations and heritability estimates obtained for the radius, spine, and hip in the young women in this study (mean age of 31) are comparable to those reported by others.[1-4] The range of heritability values among the different skeletal sites in this group of families and in other populations may simply reflect measurement variability. However, the range may also reflect the belief that some sites are more responsive to specific environmental influences than others.[9]

Kelly et al.[39] questioned the assumption that peak bone density is higher among men than women. In their study of male and female fraternal twins, women had greater hip and spine densities when corrected for body mass index. Only at the radius was density higher in men than women. Interestingly, we also failed to see a higher spine density in men after controlling for weight and height, but sex differences at the other sites remained as expected.

Alcohol consumption in this group of family members was light among daughters to moderate among all others,[40] and the prevalence of smoking was lower than average.[41] Most individuals consumed a level of calcium near or in excess of the Recommended Dietary Allowances.[42] Some similarities in physical activity, caffeine intake, alcohol consumption, and smoking at these levels were observed. In addition to parents, pressures from peers and society influence smoking, drinking, and physical activity habits.[31] It is not surprising, then, that concordance of some life-style habits between relatives was lacking. Also, a greater degree of resemblance between relatives may occur at different consumption and activity levels.

Environmental factors evaluated in this study were selected because of associations, some well established, others putative, in other populations. Conflicting findings have been reported for alcohol consumption. Positive cross-sectional associations with alcohol have been found at the spine[28] but both positive and negative associations reported at the hip.[26-28] Among mothers, alcohol consumption was directly related to heel density. Among daughters, caffeine intake showed a positive relationship with radius density, a finding similar to that seen at the hip by Cooper et al.[43] A detrimental effect of caffeine has also been reported.[44] Smoking was inversely related to BMD at two sites among daughters, supporting findings in young and older women.[22-24] Contrary to expectations, calcium intake was inversely related to spine density

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TABLE 6. ESTIMATES OF HERITABILITY BEFORE AND AFTER ADJUSTMENT FOR LIFE-STYLE[a]

	Mean offspring			*Daughters*			*Sons*		
	Before	*After*	*Difference*	*Before*	*After*	*Difference*	*Before*	*After*	*Difference*
Total body	0.69			0.65	0.58	−0.07	0.74		−0.11
Radius	0.51			0.62	0.53	−0.09	0.42		−0.02
Os calcis	0.64			0.64	0.61	−0.03	0.67		−0.16
Femoral neck	0.70			0.48	0.41	−0.07	0.91		−0.08
Spine	0.50			0.48	0.41	−0.07	0.52		−0.06

[a]Each heritability estimate is the coefficient of regression of the midparent bone density Z score on offspring Z score. Before heritabilities were computed with Z scores adjusted only for age, weight, and height. After heritabilities were computed with Z scores adjusted for age, weight, height, and the variables listed in Table 4. Each heritability estimate is significantly greater than 0 ($p < 0.05$), except those after adjustment for the femoral neck among daughters ($h_N^2 = 0.41$, $p = 0.07$) and spine among daughters ($h_N^2 = 0.41$, $p = 0.06$).

among daughters. Reproductive factors were found to influence bone density as well. Among the mothers, the length of breast-feeding was directly related to density of the heel and the hip. A similar association at the radius in postmenopausal women was reported by Hansen et al.[24] The number of live births was inversely associated with density among the mothers and daughters at several sites. Among daughters, the relationship was not due to age differences between nulliparous and parous women because bone density was standardized for age. The significance of this finding is also unknown in this particular group of mothers, all of whom had at least two children.

Caution must be taken when interpreting the significance of these environmental factors in relation to bone density. The levels of dietary factors, smoking, alcohol, and, to some extent, physical activity reflected recent exposure. Long-term exposure to any or all of these factors is expected to have an even greater effect on bone density, but cumulative histories cannot be reliably predicted from current levels in all individuals. These environmental factors were important in explaining nonheritable variance in BMD in this group of families, but it is difficult to generalize their impact to other populations.

In conclusion, this study has found evidence for a strong familial resemblance of bone density. We estimate that a significant proportion of variance in bone density in these families, approximately 46–62%, could be attributed to heredity. The remaining proportion, in the range of 38–54%, was attributable to nonheredity factors of measurement error and individual environment. Although the contribution of heredity is substantial, the impact of environment, including life-style, is also potentially large.

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